Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Monotrim 100 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 mg trimethoprim.

Excipient(s) with known effect:
Each tablet contains 24 mg lactose monohydrate.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets.

White, round tablet with a single score line separating the identifying code ($\frac{AE}{2}$) on one side.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of infections caused by trimethoprim-sensitive organisms including urinary and respiratory tract infections and prophylaxis of recurrent urinary tract infections.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Posology

1. Treatment of respiratory and urinary tract infections:

Adults and children over 12 years: 200 mg twice daily for 7 - 10 days.

The first dosage on the first day can be doubled.

2. Prophylaxis of recurrent urinary tract infection:

Adults and children over 12 years: The usual dose is 100 mg at night.

An extra 100 mg may be taken in the morning, if necessary.

3. Dosage in renal impairment:

eGFR (ml/min)	Dosage advised
Over 30	Normal
15-30	Normal for 3 days then half dose
Under 15	Half normal dose

Monitoring of renal function and serum electrolytes should be considered particularly with longer term use, in patients with impaired renal function.

Trimethoprim should only be initiated and used in dialysis patients under close supervision from specialists in both infectious disease and renal medicine. Trimethoprim is removed by dialysis.

Monitoring trimethoprim plasma concentration may be considered with long term therapy but the value of this in individual cases should first be discussed with specialists in infectious disease and renal medicine.

Paediatric population
Monotrim 100 mg Tablets are not recommended for use in children below age 12 years. Other suitable formulations (e.g. Monotrim 10 mg/ml Suspension) are available for this patient population.

Method of administration
For oral use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
Pregnancy (see section 4.6).
Premature infants and neonates under 6 weeks (see section 4.2).
Blood dyscrasias.
Severe hepatic insufficiency.

4.4 Special warnings and precautions for use

Severe cutaneous adverse reactions (SCARs)
Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported in association with trimethoprim treatment (see section 4.8).

Patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, trimethoprim should be withdrawn immediately and an alternative treatment considered (as appropriate).

If the patient has developed a serious reaction such as SJS, TEN or DRESS with the use of trimethoprim, the treatment must not be restarted in this patient at any time.

Prolonged use of an anti-infective may result in the development of superinfection due to organisms resistant to that anti-infective.

Trimethoprim may cause a depression of haemopoiesis. During long-term therapy haematology should be monitored regularly in order to detect possible pancytopenia. Particular attention should be paid to patients showing a tendency to folate deficiency (e.g. the elderly), which may be aggravated by the use of this agent. Particular care should be exercised in the haematological monitoring of children on long term therapy.If there is evidence of folic acid deficiency, calcium folinate should be administered and adequate response should be ensured by appropriate haematological monitoring. This treatment may not be effective unless trimethoprim is discontinued.

In patients with impairment of renal function, care should be taken and dose adjustment should be considered according to the severity of the conditionto avoid accumulation of trimethoprim (see section 4.2). Monitoring of renal function and serum electrolytes should be considered particularly with longer term use.

Trimethoprim should only be initiated and used in dialysis patients under close supervision from specialists in both infectious disease and renal medicine.

Special monitoring of serum electrolytes should be performed in risk patients due to risk of hyperkalaemia (see section 4.8). Elevations in serum potassium have been observed in some patients treated with trimethoprim. Patients at risk for the development of hyperkalaemia include those with renal insufficiency, poorly controlled diabetes mellitus, or those using concomitant potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes, renin angiotensin system inhibitors (e.g.: ACE inhibitors or renin angiotensin receptor blockers), or those patients taking other drugs associated

with increases in serum potassium (e.g. heparin). If concomitant use of the above-mentioned agents is deemed appropriate, monitoring of serum potassium is recommended because of the risk of severe hyperkalaemia (see section 4.5).

Blood glucose should be monitored if used concomitantly with repaglinide (see section 4.5).

Trimethoprim should be avoided in patients with porphyria.

Excipients
This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Folate antagonists and anticonvulsants: Trimethoprim may induce folate deficiency in patients predisposed to folate deficiency such as those taking folate antagonists or anticonvulsants.

Bone marrow depressants: Trimethoprim may increase the potential for bone marrow aplasia. Cytotoxics such as azathioprine, mercaptopurine, methotrexate, increase the risk of haematological toxicity when given with trimethoprim.

Phenytoin and Digoxin: Careful monitoring of patients treated with digoxin or phenytoin is advised as trimethoprim may increase plasma concentration of digoxin and phenytoin by increasing their elimination half-life.

Diuretics: In elderly patients concurrently taking diuretics, primarily thiazides, an increased incidence of thrombocytopenia with purpura has been reported. Rare cases of hyponatraemia have been reported in patients treated with trimethoprim and potassium sparing diuretics and/or thiazide diuretics.

Concomitant use of drugs that may increase serum potassium levels may lead to a significant increase in serum potassium. Potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes, renin-angiotensin system inhibitors (e.g.: ACE inhibitors or renin angiotensin receptor blockers) and other potassium increasing substances (e.g.: heparin) and aldosterone antagonists (eplerenone). Monitoring of potassium should be undertaken as appropriate (see section 4.4).

Ciclosporin: Ciclosporin may increase nephrotoxicity of trimethoprim.

Anticoagulants: The anticoagulatory effect of warfarin and other coumarins may be increased when taken together with trimethoprim.

Procainamide: Trimethoprim increases plasma concentration of procainamide.

Lamivudine: Trimethoprim may increase the plasma concentration of lamivudine.

Oral typhoid vaccine: This is inactivated by concomitant administration of anti-bacterials.

Pyrimethamine: The anti-folate effect may be increased if there is concomitant administration with trimethoprim.

Dapsone: Plasma concentrations of trimethoprim and dapsone may increase when taken together.

Repaglinide: Trimethoprim may enhance hypoglycaemic effect of repaglinide (see section 4.4).

Rifampicin may decrease trimethoprim concentration.

Dofetilide: Serum levels can be increased when co-administered with trimethoprim.

Other: Increased risk of haematological toxicity with azathioprine, methotrexate, mercaptopurine and pyrimethamine.

Trimethoprim may interfere with diagnostic tests including serum methotrexate assay where dihydrofolate reductase is used and the Jaffe reaction for creatinine.

4.6 Fertility, pregnancy and lactation

Pregnancy
Trimethoprim should not be used during pregnancy.

Epidemiological studies have shown an increased risk of spontaneous abortion and congenital malformations, in particular neural tube defects, oral clefts and cardiovascular defects, in children of mothers treated with trimethoprim during the first trimester of pregnancy. The presumed mechanism of action is thought to be interference with folates.

Breast-feeding
Trimethoprim is excreted in breast milk. This should be kept in mind when considering administration to lactating women.

4.7 Effects on ability to drive and use machines

Monotrim 100 mg Tablets has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The frequencies of the undesirable effects listed below are categorised as follows:
Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

Infections and infestations
Common: Candidiasis, Clostridium difficile colitis.
Not known: Aseptic meningitis.
Aseptic meningitis recurred in a number of cases on re-exposure to either co-trimoxazole or to trimethoprim alone.

Blood and lymphatic system disorders
Very rare: Thrombocytopenia, anaemia, neutropenia, eosinophilia, leukopenia, pancytopaenia, bone marrow depression, agranulocytosis, aplastic anaemia, haemolytic anaemia, haemolysis
Not known: Depression of haemopoiesis (see sections 4.4, 4.5)

Fatalities have been reported (especially in the elderly, or those with impairment of renal or hepatic function in whom careful monitoring is advised (see sections 4.3, 4.4), however the majority of haematological changes are mild and reversible when treatment is stopped. Use in severe hepatic insufficiency is contraindicated (see section 4.3).

Immune system disorders
Not known: Hypersensitivity, anaphylaxis, angioedema, allergic vasculitis resembling Henoch-Schoenlein purpura

Metabolism and nutrition disorders
Very common: Hyperkalaemia.
Not known: Hyponatraemia
Close supervision is recommended when trimethoprim is used in elderly patients or in patients taking high doses as these patients may be more susceptible to hyperkalaemia and hyponatraemia.

Psychiatric disorders
Very rare: Agitation, hallucinations
Not known: Depression, anxiety, abnormal behaviour, confusional states, insomnia and nightmares

Nervous system disorders
Common: Headache
Very rare: Lethargy, dizziness
Not known: Dyskinesias, tremor, ataxia, syncope, paraesthesiae, peripheral neuritis

Eye disorders
Not known: Uveitis.

Respiratory, thoracic and mediastinal disorders

Not known: Cough, wheezing, epistaxis

Gastrointestinal disorders
Very common: Diarrhoea, decreased appetite
Common: Sore mouth
Very rare: Constipation, glossitis, stomatitis, pancreatitis
Not known: Gastrointestinal upset, nausea, vomiting

Hepatobiliary disorders
Not known: Disturbances of liver enzyme values, jaundice, hepatic necrosis, which may be fatal.

Skin and subcutaneous tissue disorders:
Very rare: Fixed drug eruption, exfoliative dermatitis, bullous dermatitis
Not known: Rash, pruritus, photosensitivity, erythema multiforme, Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), urticaria, erythema nodusum

Musculoskeletal and connective tissue disorders:
Not known: Myalgia

Renal and urinary disorders
Not known: Impaired renal function (sometimes reported as renal failure), haematuria. Trimethoprim may affect haemopoiesis (See sections 4.4 and 4.5)

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

Symptomatic treatment, gastric lavage and forced diuresis can be used. Depression of haematopoiesis by trimethoprim can be counteracted by intramuscular administration of calcium folinate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Trimethoprim and derivatives, ATC code: J01EA01

Trimethoprim is an antimicrobial agent.

Mechanism of action
The antimicrobial activity is due to selective inhibition of bacterial dihydrofolate reductase. In-vitro trimethoprim has effect on most Gram-positive and Gram-negative aerobic organisms, including enterobacteria such as *E.coli, Proteus, Klebsiella pneumoniae, Streptococcus faecalis, Streptococcus pneumoniae, Haemophilus influenzae*, and *Staphylococcus aureus*.

It has no effect on *Mycobacterium tuberculosis, Neisseria gonorrhoeae, Pseudomonas aeruginosa, Treponema pallidum, Brucellaabortis* or anaerobic bacteria.

Susceptibility testing breakpoints minimum inhibitory concentration (MIC) interpretive criteria for susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for trimethoprim and are listed here: https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx".

5.2 Pharmacokinetic properties

Absorption and Biotransformation

Trimethoprim is absorbed rapidly and almost completely after oral administration and maximum plasma concentrations are reached after 1- 4 hours. Peak plasma concentration of about 1 µg per ml has been reported after a single dose of 100 mg.

Half-life is about 12 hours in patients with normal renal function but up to 20 - 50 hours in anuric patients.

Distribution
Trimethoprim is rapidly and widely distributed to various tissues and fluids, including kidneys, liver, spleen, bronchial secretions, saliva and prostatic tissue and fluid. Tissue concentration is generally higher than plasma concentration.

Elimination
About 40 to 50% of a trimethoprim dose is excreted in the urine within 24 hours mainly as unchanged drug, hence patients with impaired renal function, such as the elderly, may require a reduction in dosage due to accumulation. Trimethoprim appears in breastmilk. Urinary concentrations are generally well above the MIC of common pathogens for more than 24 hours after the last dosage.

5.3 Preclinical safety data

Not relevant (widely used in clinical practice).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Potato starch
Talc
Gelatin
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

HDPE tablet container with LDPE closure.
100 and 500 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Chemidex Pharma Limited
Vision Exchange Building
Triq it-Territorjals, Zone 1
Central Business District

Birkirkara
CBD 1070
Malta

8 MARKETING AUTHORISATION NUMBER

PA22643/002/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

April 2026